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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/009,950	12/14/2001	Akira Nakamura	31671-176197	7278

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EXAMINER	
BERTOGLIO, VALARIE E	

ART UNIT	PAPER NUMBER
1632	

DATE MAILED: 03/23/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/009,950	NAKAMURA ET AL.	
	Examiner	Art Unit	
	Valarie Bertoglio	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *17 January 2005*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1 and 3* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1 and 3* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *12/14/2001* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Applicant's reply filed 01/17/2005 has been received. Claims 2-4 and 11 have been cancelled. Claims 1 and 3 have been amended, are pending, and are under consideration.

Claim Objections

The objection to claim 3 is withdrawn.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

The rejection of claims 1 and 3 is maintained under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a transgenic mouse whose genome comprises a homozygous disruption of the exons encoding S_2 and EC_1 of the FcγRIIB gene wherein immunization of said transgenic mouse with type IV collagen results in a mouse model of Goodpastures syndrome exhibiting diffuse alveolar hemorrhage, glomerulonephritis and the appearance of antikidney glomerular basement membrane antibody and for a method of using the claimed mouse to screen for potential remedies, does not reasonably provide enablement for destruction or deficiency of the FcγRIIB gene. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims. Applicant's arguments have been thoroughly considered and are found partially persuasive.

Claim 1 is directed to a mouse model of Goodpastures syndrome wherein the genome of the mouse comprises a disruption of the FcγRIIB gene and is immunized with type IV collagen

resulting in a phenotype of diffuse alveolar hemorrhage, glomerulonephritis and the appearance of antikidney glomerular basement membrane antibody. Claim 3 encompasses a method of using the claimed mouse for screening for remedies for symptoms of Goodpastures syndrome that are exhibited by the mouse.

The aspect of the scope of enablement rejection regarding the Markush language and the breadth of the phenotypes encompassed by the claims is withdrawn in light of Applicant's amendments to the claims. The aspect of the rejection with respect to the method of claim 3 not being enabled for using a wild-type as a control mouse in the method is withdrawn in light of Applicant's amendments to the claim.

The aspect of the rejection with respect to the breadth of the type of genetic mutation is maintained for reasons of record as set froth on pages 3-4 of the previous office action mailed 10/19/2004.

The breadth of the claims is such that they encompass genetic mutation of the FcγRIIB gene by any type of destruction, deficiency or substitution. However, the specification and the art of record teach only substitution of the exons S_2 and EC_1 with a neo gene cassette (see specification page 9, paragraph 3; Takai, 1996, Nature, Vol. 379, page 347, Figure 1a, IDS). The specification does not teach any other sort of genetic disruption involving the FcγRIIB gene. Other gene disruptions, including substitution of other domains or exons will not necessarily cause the same change in activity of the FcγRIIB gene product as the disruption taught by the specification. It cannot be predicted what activity level and what phenotype a resulting mouse would have with any other gene disruption. Therefore, it would require undue experimentation for the skilled artisan to make the claimed mouse having any type of destruction, deficiency or

substitution other than substitution of the exons S_2 and EC_1 with a neo gene cassette as taught by the instant specification.

Claim Rejections - 35 USC § 112-2nd paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

The rejection of claim 3 under 35 USC 112, 2nd paragraph, is withdrawn in light of Applicant's amendments to the claim.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The rejection of claim 1 under 35 U.S.C. 103(a) as being unpatentable over Takai (1996, Nature, Vol. 379, pages 346-348; IDS) in view of Abbate, (1998, Kidney International, Vol. 54, pages 1550-1561; IDS) or Kalluri (1994, PNAS, Vol. 91, pages 6201-6205;IDS) is maintained for reasons of record set forth on pages 6-7 of the previous office action. Applicant's arguments have been fully considered and are not found persuasive.

Applicant has argued that the animals, mice and rats, of Abbate and of Kalluri immunized with type IV collagen are not satisfactory as models of Goodpasture's syndrome because they do not exhibit all of the claimed symptoms to the appropriate degree.

In response, the rejection is based on the combination of teachings of Takai and Abbate or of Takai and Kalluri. The symptoms observed by Abbate and by Kalluri are taught to be those

of Goodpasture's syndrome. The fact that the symptoms are weaker than desired in a model presents motivation to enhance they effects of immune reaction to the type IV collagen by weakening the negative response of the animals to autoimmunity by knocking out the FcγRIIB gene as taught by Takai. Takai taught that the FcγRIIB gene encodes a low-affinity immunoglobulin-G receptor that acts as a general negative regulator of immune-complex triggered immune system activation. Loss of this negative-regulator increased humoral and anaphylactic responses in the mice because the mice lack an ability for regulation of antibody level in response to antigenic stimulation (page 347, col. 1, last paragraph).

Applicant argues that Abbate used a rat not a mouse. In response, the species of mammal used by Abbate is of little significance. Kalluri used mice and it would be obvious to use mice in combining the teachings of Takai and Kalluri or Takai and Abbate because gene targeting technology, at the time the invention was made, was limited to mouse.

Therefore, that the model animals known and characterized as exhibiting symptoms of Goodpasture's syndrome exhibited weaker phenotypes than the mice of the instant invention does not overcome the obviousness rejection. The symptoms of the animals in the art were strong enough to make the correlation to Goodpasture's syndrome. 35 USC 103(a) does not require that a single reference alone teach the invention as claimed. Therefore, the rejection is maintained.

Conclusion

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Valarie Bertoglio whose telephone number is (571) 272-0725. The examiner can normally be reached on Mon-Thurs 5:30-4:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ram Shukla can be reached on (571) 272-0735. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Valarie Bertoglio
Examiner
Art Unit 1632

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